

#19

PTO/SB/64 (08-03)

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**PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED
UNINTENTIONALLY UNDER 37 CFR 1.137(b)**

Docket Number (Optional)

R-477

First named inventor: ALLEN

Application No.: 09/904,180

Art Unit: 1636

Filed: 07/11/01

Examiner: DANIEL M. SULLIVAN

Title: TRANSGENIC MICE CONTAINING STEFIN
HOMOLOG PROTEASE INHIBITOR GENE DISRUPTIONS

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Attention: Office of Petitions

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APPLICANT HEREBY PETITIONS FOR REVIVAL OF THIS APPLICATION

NOTE: A grantable petition requires the following items:

- (1) Petition fee;
- (2) Reply and/or issue fee;
- (3) Terminal disclaimer with disclaimer fee --required for all utility and plant applications
filed before June 8, 1995; and for all design applications; and
- (4) Statement that the entire delay was unintentional.

1. Petition fee

☒ Small entity-fee \$ 665.00 (37 CFR 1.17(m)). Applicant claims small entity status. See 37 CFR 1.27.

☐ Other than small entity - fee \$ _____ (37 CFR 1.17(m))

2. Reply and/or fee

A. The reply and/or fee to the above-noted Office action in

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☐ has been filed previously on _____

☒ is enclosed herewith.

B. The issue fee of \$ _____

☐ has been paid previously on _____

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10/28/2003 AMONDAF1 00000171 501271 09904180

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[Page 1 of 2]

This collection of information is required by 37 CFR 1.137. The information is required to obtain or retain a benefit by the public which is to file (and by the
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- ☐ A terminal disclaimer (and disclaimer fee (37 CFR 1.20(d)) of \$ _____ for a small entity or \$ _____ for other than a small entity) disclaiming the required period of time is enclosed herewith (see PTO/SB/63).

4. STATEMENT: The entire delay in filing the required reply from the due date for the required reply until the filing of a grantable petition under 37 CFR 1.137(b) was unintentional. [NOTE. The United States Patent and Trademark Office may require additional information if there is a question as to whether either the abandonment or the delay in filing a petition under 37 CFR 1.137(b) was unintentional (MPEP 711.03(c), subsections (III)(C) and (D))].

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Date

Kelly L. Quast

Signature

Telephone

Number: 650-569-5100

KELLY L. QUAST

Typed or printed name

1031 BING STREET

Address

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SAN CARLOS, CA. 94070

Address

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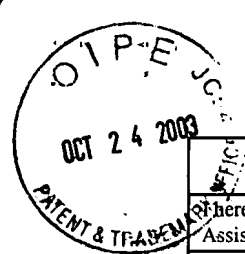
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PETITION TO REVIVE UNDER 37 C.F.R. §1.137(b) Address to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Application Number	09/904,180
	Confirmation Number	1187
	Filing Date	July 11, 2001
	First Named Inventor	Keith D. Allen
	Examiner	Daniel M. Sullivan
	Group Art	1636
	Title	Transgenic Mice Containing Stefin Homolog Protease Inhibitor Gene Disruptions
	Attorney Docket No.	R-477

Sir:

The above referenced application has unintentionally fallen abandoned due to the inadvertent failure to timely file a proper reply to the Office Action mailed January 14, 2003. A reply was filed April 14, 2003, which was not considered by the Examiner to place the application in condition for allowance, and therefore was not entered (see Advisory Action mailed May 7, 2003). Applicant unintentionally failed to file an amendment responsive to the Advisory Action within the six month statutory period ending July 14, 2003.

In order to revive the status of the application, attached herewith is a Petition for Revival of an unintentionally Abandoned Application under 37 C.F.R. § 1.137(b). Applicant hereby states that the entire delay in responding to the outstanding Office Action was unintentional. Applicant also submits the following Amendment in response to the Office Action dated January 14, 2003, and requests entry and consideration of the following amendments and remarks upon reinstatement of the application to active status. In view of the amendments to the claims and the remarks set forth below, reconsideration and allowance are respectfully requested.

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AMENDMENTS TO THE CLAIMS

Following is a complete listing of the claims, including any amendments. Please amend the claims to read as indicated below. Amendments to the claims are shown in reference to the version of the claims examined in the Office Action mailed January 14, 2003.

1. (Currently Amended) A targeting construct ~~capable of homologous recombination with SEQ ID NO: 1~~, comprising:
 - (a) a first polynucleotide sequence homologous to a at least a first portion of an endogenous mouse stefin homolog gene comprising SEQ ID NO:1;
 - (b) a second polynucleotide sequence homologous to at least a second portion of the stefin homolog gene; and
 - (c) a selectable marker located between the first and second polynucleotide sequences;
wherein where said targeting construct is introduced into a mouse embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.
2. (Original) The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. (Currently Amended) A method of producing a targeting construct ~~capable of homologous recombination with SEQ ID NO: 1~~, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to a at least a first portion of an endogenous mouse stefin homolog gene comprising SEQ ID NO:1;
 - (b) providing a second polynucleotide sequence homologous to at least a second portion of the stefin homolog gene;
 - (c) providing a selectable marker located between the first and second polynucleotide sequences; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. (Currently Amended) A method of producing a targeting construct ~~capable of homologous recombination with SEQ ID NO: 1~~, the method comprising:

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- (a) providing a polynucleotide comprising a first sequence homologous to a first region of an endogenous mouse stefin homolog gene comprising SEQ ID NO:1 and a second sequence homologous to a second region of a the stefin homolog gene; and
- (b) inserting a positive selection marker between the first and second sequences to form the targeting construct

wherein where said targeting construct is introduced into a mouse embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.

5. (Currently Amended) A mouse embryonic stem cell comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO:1, wherein said cell, when introduced into a blastocyst produces a transgenic mouse comprising a genome having a disruption in the stefin homolog gene, wherein where the mouse is homozygous for the disruption, the mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder ~~target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO:1.~~

Claim 6 is canceled.

Claim 7 is canceled.

8. (Currently Amended) A transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1, wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of: increased activity and a neuropsychological disorder ~~target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO:1.~~

9. (Currently Amended) A cell derived from the ~~non-human~~ transgenic mouse ~~animal~~ of claim 8.

10. (Currently Amended) A method of producing a transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ

~~ID NO: 1 target gene sequence disrupted by homologous recombination of the target gene sequence with a sequence homologous to a region of SEQ ID NO: 1, the method comprising:~~

- (a) introducing the targeting construct of claim 1 into a mouse embryonic stem cell;
- (b) introducing the cell into a blastocyst;
- (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
- (d) breeding the chimeric mouse to produce the transgenic mouse wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of: increased activity and a neuropsychological disorder.

11. (Currently Amended) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a stefin homolog gene comprising SEQ ID NO:1 ~~modulates the expression of a stefin homolog~~, the method comprising:

- (a) providing the transgenic mouse of claim 8;
- (b) administering an agent to the transgenic mouse ~~non-human transgenic animal~~; and
- (c) determining whether the ~~expression of stefin homolog in the mouse~~ phenotype is ameliorated modulated.

Claims 12-19 have been canceled.

20. (Currently Amended) The transgenic mouse of claim 8 ~~18~~, wherein the increased activity is characterized by increased velocity of movement in an open-field test, ~~relative to a wild-type mouse.~~

21. (Currently Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises a transgenic mouse exhibits decreased propensity for despair or depression, ~~relative to a wild-type mouse.~~

22. (Currently Amended) The transgenic mouse of claim 21, wherein the decreased propensity for despair or depression is characterized by a decreased amount of time spent immobile when tail suspended ~~time in a tail suspension test, relative to a wild-type mouse.~~

23. (Currently Amended) The transgenic mouse of claim 8, wherein the

neuropsychological disorder comprises ~~transgenic mouse exhibits~~ a stimulus-processing deficit ~~relative to a wild-type mouse~~.

24. (Currently Amended) The transgenic mouse of claim 23-18, wherein the stimulus-processing deficit is characterized by decreased pre-pulse inhibition.

25. (Currently Amended) The transgenic mouse of claim 24-8, wherein the decreased pre-pulse inhibition is consistent with ~~transgenic mouse exhibits~~ schizophrenic behavior.

Claims 26-32 have been canceled.

REMARKS

Formal Matters

Claims 1-11, 13, 18-26 and 28-32 were examined. Claims 1-11, 13, 18-26 and 28-32 were rejected in the final Office Action dated January 14, 2003. The response to this Office Action was not entered by the Examiner, as noted in the Advisory Action dated May 7, 2003. The Examiner noted in the Advisory Action that claims 1-4, 8, 9, 11 and 20-25 as filed in the response dated April 14, 2003 would be allowable if submitted in a separate amendment.

Claims 1-5, 8-11 and 20-25 are pending after entry of the amendments set forth herein. Claims 1, 3, 4, 8-11 and 20-25 have been amended in the form filed in the response dated April 14, 2003, which were considered responsive to the Office Action and to be allowable (see Advisory Action). Claims 5, 10 and 13 have been amended and/or canceled in a genuine effort to place the claims in conditions for allowance in response to the concerns and/or suggestions set forth by the Examiner in the Advisory Action. Claims 6-7, 12-19 and 26-32 have been canceled by this amendment.

Support for the amendments to claims 1-5 and 8-11 can be found throughout the specification, at, for example, page 3, line 14, page 6, lines 19 and 22-24, page 11, line 19 through page 15, line 28. Support for the amendments to claims 20-25 can be found throughout the specification, at, for example, page 3, line 14, page 6, lines 19 and 22-24, page 14, lines 14-20 and page 51, line 10 through page 53, line 16. As such, no new matter has been added.

The foregoing amendments have been made in a genuine effort to place the claims in condition for allowance, and are not intended to limit the scope of the invention. Applicant has attempted to respond to the Examiner's concerns and/or adopt the Examiner's suggestions for placing the claims in allowable form, including those set forth in the Advisory Action dated May 7, 2003. Amendments to the claims, including cancellation of claims, are made without prejudice to the pending or now canceled claims or to any subject matter pursued in a related application. The Applicant reserves the right

to prosecute any canceled subject matter at a later time or in a later filed divisional, continuation, or continuation-in-part application.

For the Examiner's convenience, attached herewith is Appendix A, containing a clean copy of all pending claims. Applicant is aware that the new rules regarding amendments do not require clean versions of amended claims, but provide this Appendix due to the Examiner's requests for clean versions of certain claims in the Office Action dated January 14, 2003 and Advisory Action dated May 7, 2003.

Applicant respectfully requests reconsideration of the application in view of the amendments and remarks made herein.

Rejection under 35 U.S.C. § 112, 1st paragraph (enablement).

Claims 5-11, 13, and 18-26 stand rejected, and new claims 28-32 are rejected under 35 U.S.C. § 112, first paragraph for allegedly lacking enablement for the full scope of the claims.

Claims 5, 8 and 10 have been rejected for assertedly being non-enabling because the "disrupted gene need not comprise the sequence set forth as SEQ ID NO: 1." (Office Action dated January 14, 2003, page 3) The Office Action asserted that "the specification is enabling for a homozygous knockout mouse comprising a disruption in the stefin homolog gene set forth in SEQ ID NO: 1 and exhibiting phenotypic features . . . as compared to wild-type mice." However, according to the Examiner, these claims encompass products and methods comprising disruption of any gene that is homologous to a sequence that is homologous to a region of SEQ ID NO:1, and the cells and animals recited by these claims need not comprise a disruption resulting in an enabled phenotype. Claims 5, 8 and 10, as amended herein, are now directed to a cell or transgenic mouse having a stefin homolog gene comprising SEQ ID NO: 1, which cell (when used to produce a transgenic mouse) or transgenic mouse, when homozygous for the disruption, exhibits a phenotype of increased activity or a neuropsychological disorder. As such, the Applicant submits that the rejections are overcome by the amendment and respectfully requests that these rejections be withdrawn.

Claims 5, 6 and 13 have been asserted to be non-enabling "for any cell other than

a cell derived from the transgenic mouse or a mouse ES cell.” (Office Action dated January 14, 2003, page 4) The Office Action also asserted that “the disclosure is enabling only for a cell derived from a KO mouse . . . [and] for an ES cell.” The Examiner asserted in the Advisory Action dated May 7, 2003 that use of the term “murine embryonic stem cell” would encompass a rat embryonic stem cell, the use of which in the claimed methods is allegedly not enabled by the specification. Applicant has amended claim 5 to recite a “mouse embryonic stem cell” which the Examiner has noted is enabled by the specification. Claims 6 and 13 have been canceled. Thus, the Applicant submits that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Claims 11 and 13 have also been asserted to be non-enabling for “a method by which expression of a gene that has been disrupted can be measured.” (Office Action dated January 14, 2003, page 4) The Office Action also asserted that “the specification is enabling for ‘a method of identifying an agent that modulates the expression and/or function of a stefin [homolog gene] and thereby ameliorates a phenotype associated with the disruption.’” Claim 11 encompasses the phenotypes of stem cells and/or transgenic mouse of claims 5 and 8. The Applicant has canceled claim 13, and amended claim 11 to be drawn to a method for identifying an agent that ameliorates the encompassed phenotypes. Applicant notes that the Examiner has stated in the Advisory Action that claim 11 would be allowed if submitted in a timely filed amendment. As such, the Applicant submits that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Claim 10 has been rejected for assertedly being non-enabling because “neither the instant disclosure nor the prior art provide enablement for a method of producing a transgenic mouse from any cell other than a mouse ES cell.” (Office Action dated January 14, 2003, page 5) The Examiner has further stated that the specification does not enable such a method wherein “the method is not limited to a useful phenotype...” (Advisory Action dated May 7, 2003, page 2). The Applicant has amended claim 10 to recite using a mouse embryonic stem cell and has limited the claim to a method of producing the transgenic mouse having the phenotypes enabled by the specification. As

such, the Applicant submits that the rejections are overcome by this amendment and respectfully request that these rejections be withdrawn.

Therefore, Applicant submits that the rejection of the above-cited claims under 35 U.S.C. § 112, first paragraph, is overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw this rejection. Applicant submits that claims 1-5, 8-11 and 20-25 are enabled by the instant specification.

Rejection under 35 U.S.C. § 112, 1st paragraph (possession).

Claims 1-11, 13, 18-26 and 28-32 have been rejected under 35 U.S.C. § 112, first paragraph, for assertedly not being adequately described in the disclosure. Claims 6-7, 12-19 and 26-32 have been canceled by this amendment.

The Office Action asserts that targeting constructs “comprising all or a portion of the sequence set forth in SEQ ID NO: 1, methods of using said targeting constructs comprising all or a portion of the sequence set forth as SEQ ID NO: 1 and mice and cells comprising a disruption of the stefin homolog gene comprising the sequence set forth as SEQ ID NO: 1 meet the written description provision of 35 U.S.C. § 112, first paragraph.” (Office Action dated January 14, 2003, page 6) Applicant submits that the rejections are overcome by this amendment and respectfully requests that these rejections be withdrawn.

Therefore, Applicant submits that the rejection of the above-cited claims under 35 U.S.C. § 112, first paragraph, is overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw this rejection.

Rejection under 35 U.S.C. § 112, 2nd paragraph.

Claims 1-4 and 9-13 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

The Office Action asserts that claim 9 is indefinite for being directed to a non-human transgenic animal because there is no antecedent basis in claim 8 for any transgenic animal other than a mouse. The Office Action suggests that “amending the claim such that it is directed to a cell derived from the transgenic mouse of claim 8 would

overcome this rejection.” The Applicant has adopted this suggestion.

The Advisory Action states that “the proposed amendment [in the response filed April 14, 2003] to claim 5 raises new grounds for rejection of claims 5 and 13 under 35 U.S.C. § 112, first **and second** paragraphs” due to use of the term murine. As noted above, Applicant has amended claim 5 to recite a mouse embryonic stem cell, which should overcome this concern raised by the Examiner.

Therefore, Applicant submits that the rejection of the above-cited claims under 35 U.S.C. § 112, second paragraph, is overcome in view of the amendments and remarks set forth herein. The Examiner is thus respectfully requested to withdraw this rejection.

Conclusion.

Applicant has attempted to address each and every issue raised by the Examiner in both the Office Action (dated January 14, 2003) and the Advisory Action (dated May 7, 2003) in response to the “Amendment” filed April 14, 2003. Applicant submits that upon entry of the amendment and consideration of the remarks contained therein, all of the pending claims are in condition for allowance, which action is respectfully requested.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1271 under order No. R-477.

Respectfully submitted,
DELTAGEN, INC.

Date: October 17, 2003

By: Kelly L. Quast
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Appendix A

1. (Currently Amended) A targeting construct comprising:
 - (a) a first polynucleotide sequence homologous to at least a first portion of an endogenous mouse stefin homolog gene comprising SEQ ID NO: 1;
 - (b) a second polynucleotide sequence homologous to at least a second portion of the stefin homolog gene; and
 - (c) a selectable marker located between the first and second polynucleotide sequences;wherein where said targeting construct is introduced into a murine embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.
2. (Original) The targeting construct of claim 1, wherein the targeting construct further comprises a screening marker.
3. (Currently Amended) A method of producing a targeting construct, the method comprising:
 - (a) providing a first polynucleotide sequence homologous to at least a first portion of an endogenous mouse stefin homolog gene comprising SEQ ID NO: 1;
 - (b) providing a second polynucleotide sequence homologous to at least a second portion of the stefin homolog gene;
 - (c) providing a selectable marker located between the first and second polynucleotide sequences; and
 - (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.
4. (Currently Amended) A method of producing a targeting construct, the method comprising:
 - (a) providing a polynucleotide comprising a first sequence homologous to a first region of an endogenous mouse stefin homolog gene comprising SEQ ID NO: 1 and a second sequence homologous to a second region of the stefin

homolog gene; and

(b) inserting a positive selection marker between the first and second sequences to form the targeting construct;

wherein where said targeting construct is introduced into a mouse embryonic stem cell and homologously recombines with the stefin homolog gene, said homologous recombination disrupts the stefin homolog gene.

5. (Currently Amended) A mousee embryonic stem cell comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1; wherein said cell, when introduced into a blastocyst produces a transgenic mouse comprising a genome having a disruption in the stefin homolog gene, wherein where the mouse is homozygous for the disruption, the mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder.

Claim 6 is canceled.

Claim 7 is canceled.

8. (Currently Amended) A transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1; wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of increased activity and a neuropsychological disorder.
9. (Currently Amended) A cell derived from the transgenic mouse of claim 8.
10. (Currently Amended) A method of producing a transgenic mouse comprising a genome comprising a disruption in an endogenous stefin homolog gene comprising SEQ ID NO: 1, the method comprising:
- (a) introducing the targeting construct of claim 1 into a mouse embryonic stem cell;
 - (b) introducing the cell into a blastocyst;
 - (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and
 - (d) breeding the chimeric mouse to produce the transgenic mouse.

wherein where the disruption is homozygous, the transgenic mouse exhibits, relative to a wild-type mouse, a phenotype selected from the group consisting of: increased activity and a neuropsychological disorder.

11. (Currently Amended) A method of identifying an agent that ameliorates a phenotype associated with a disruption in a stefin homolog gene comprising SEQ ID NO:1, the method comprising:
- (a) providing the transgenic mouse of claim 8;
 - (b) administering an agent to the mouse; and
 - (c) determining whether the phenotype is ameliorated.

Claims 12-19 have been canceled.

20. (Currently Amended) The transgenic mouse of claim 8, wherein the increased activity is characterized by increased velocity of movement in an open-field test.
21. (Currently Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises a decreased propensity for despair or depression.
22. (Currently Amended) The transgenic mouse of claim 21, wherein the decreased propensity for despair or depression is characterized by a decreased amount of time spent immobile when tail-suspended.
23. (Currently Amended) The transgenic mouse of claim 8, wherein the neuropsychological disorder comprises a stimulus-processing deficit.
24. (Currently Amended) The transgenic mouse of claim 23, wherein the stimulus-processing deficit is characterized by decreased pre-pulse inhibition.
25. (Currently Amended) The transgenic mouse of claim 24, wherein the decreased pre-pulse inhibition is consistent with schizophrenic behavior.

Claims 26-32 have been canceled.

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underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[GNCAGCAATTCCTCTAAGGGATNCAATNNGGCTTGCCCGAGGCCACACTCATTTCCTCCA
TNCCCTCAAATACTGTGGTGATTAAACATTTTCATAGGAGGANTTTATGGATNCCTTTAAA
ANCCTAATTCTCCCTGCTTGCCAAATCATTCTTCTCAGCATCCTGCCAGCAAAAAANC
ANCTTNTGATCAAAATNATCCCCGGAGGCTTNACGGAGGCCAGACCTGCCACAGCAGN]A
GTCCNGGAGATTGCTGACCGGGTCAAAGCACAGCTCGANGAGGAAACCAATGAGAAATAT
GAAATATTCAAAGCCGTTGAGTATAAACTCAAGTTGTCGCTGGAGTCAATTACTTCATT
AAGATGGATGTAGGGGTGGTTGTTTACCCACATAAAAGTCTTCAAGGATCTTTCTGGA
AAGAATAATTTGGAATT[ACTGGTTACCAGACTAACAAAACCGAGGATGATGAGCTGAC
CTACTTCTAAGCAGCAAAATCTAAAGTGACCTGATTCCTCTCATTGTAAACTGATTTCGNC
CATCAATAAAGAATATTCTOCA] (SEQ ID NO:1)

FIGURE 2A

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